REMARKS

With this amendment, claim 5 has been cancelled and incorporated into claim 1. Claims 1 and 2 have been amended. Support for the amendments is found in the existing claims and the specification as discussed below. Accordingly, the amendments do not constitute the addition of new matter. Applicant respectfully requests the entry of the amendments and reconsideration of the application in view of the amendments and the following remarks.

Rejection under 35 U.S.C. § 112, second paragraph

Claim 2 is rejected under 35 U.S.C. § 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 2 is rejected for use of a trademark "Triton X-100". Claim 2 has been amended to include generic description. Withdrawal of the rejection is respectfully requested in view of the amendment.

Rejection under 35 U.S.C. § 103(a)

Claims 1, 3, 4, 9, and 10 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Lurquin, et al. (Analytical Biochemistry (1975) 65: 1-10) in view of Vosbeck, et al. (JBC (1973) 248 (17) : 6029-6034) and further in view of Werner, et al. (Plant Molecular Biology Reporter (1998) 16: 295-299).

The limitation from claim 5 that the sample is a blood sample has been incorporated into claim 1, from which claims 3, 4, 9 and 10 depend. As claim 5 was not subject to this ground of rejection and as the cited references are directed to *Chlamydomonas reinhardii* (Lurquin and Werner) and *Streptomyces griseus* (Vosbeck), rather than to blood cells, it is believed that this ground of rejection is addressed by the amendment.

Withdrawal of the rejection is respectfully requested.

Rejection under 35 U.S.C. § 103(a)

Claim 2 is rejected under 35 U.S.C. § 103(a) as being unpatentable over Lurquin, et al. (Analytical Biochemistry (1975) 65: 1-10) in view of Vosbeck, et al. (JBC (1973) 248 (17) :

6029-6034) and further in view of Werner, et al. (Plant Molecular Biology Reporter (1998) 16: 295-299) and further in view of Wilson, et al (US 7,045,679 B1).

The rejection based upon Lurquin, et al. Vosbeck, et al. and Werner, et al. is believed to be overcome as discussed above. As claim 2 depends from claim 1 and includes all of the limitations thereof, this ground of rejection as applied to claim 2 is also believed to be overcome. Withdrawal is respectfully requested.

Rejection under 35 U.S.C. § 103(a)

Claims 1-5, 9 and 10 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Burdick et al. (EP 0393744 A1) in view of Akane, et al. (Biotechniques (1994) 16(2): 235,237,238).

The claims have been amended to specify that the sample is a blood sample as discussed above and also to specify that the method steps are performed in the order as presented in the claim.

The inventors have discovered a means to isolate DNA of sufficient purity for PCR by a fast and efficient method. This method was not known previously as indicated by the absence of any rejection of the claims as anticipated. Although the various reagents and method steps were known, they had not been previously combined in the manner as claimed.

Furthermore, the combination of references does not teach all of the claim limitations as none of the cited references teaches the high salt concentrations of the claimed invention. The Examiner takes the position that the temperatures and salt concentrations are a matter of routine optimization.

As set forth in M.P.E.P. 2144.05:

> Applicants can rebut a *prima facie* case of obviousness based on overlapping ranges by showing the criticality of the claimed range. "The law is replete with cases in which the difference between the claimed invention and the prior art is some range or other variable within the claims. . . . In such a situation, the applicant must show that the particular range is critical, generally by showing that the claimed range achieves unexpected results relative to the prior art range." *In re Woodruff*, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990)..

With the previous response, Applicants submitted the 132 Declaration of Satoshi Majima to show criticality of the claimed range and unexpected results. As discussed previously, the

side-by-side comparison presented in the Declaration clearly shows the advantage of high salt in DNA extraction for purposes of PCR. In the Declaration, DNA was isolated in the absence of high salt concentration (item 7) and in the presence of high salt concentration (item 8) The time for these DNA isolations was the same (10 minutes). The isolated DNAs were amplified using PCR (item 9) and used for melting curve analysis (item 10, Table 1).

By the use of high salt according to the claimed method, the isolated DNA was sufficiently purified and concentrated so that the amplified DNA provided a sharp peak for Tm analysis. The DNA isolated using 0.1M NaCl (low concentration) was not sufficient for Tm analysis.

Accordingly, by the use of high salt according to the claimed method, a fast, efficient DNA isolation can be performed which can be amplified using standard techniques and used for Tm analysis. The use of the high salt concentration as claimed is critical to achieve this result, i.e. "amplify[ication] of the object DNA from the fraction containing nucleic acid by PCR", as claimed. Furthermore, the increase in salt concentration produces a dramatic difference in result which is unexpected in view of the prior art.

The Examiner found that the Declaration was not sufficient to overcome the rejection because:

1) The sample was limited to blood samples.

2) The sample was heated at only one temperature (98°C).

3) The heating time was only one time period (5 min.).

4) A specific surfactant was used.

5) A specific salt of a monovalent cation was used (NaCl).

6) The Examiner questioned whether or not the results were statistically significant.

In response, the variable being tested, (salt concentration) was tested at 3 different concentration while holding other conditions constant so that valid comparison could be made. As the Declaration sought to show criticality of the salt concentration, other variables were held constant while the salt concentration was varied.

Furthermore, the claims are now limited to "blood samples" so the Examiner's concerns with regards to point 1 have been addressed by amendment. Regarding points 2 and 3, directed to the heating temperature and heating time, as taught by the specification : "Heating temperature

is not particularly limited so long as it is a temperature at which a protein can be sufficiently denatured... Heating time is not particularly limited so long as it is a time during which proteins can be sufficiently denatured under the heating condition" (present specification, page 6, paragraph 3). Accordingly, the heating time and temperature are not critical (although it is critical to perform the heating step AFTER addition of salt as discussed in previous responses).

Regarding points 4 and 5, while Applicants did not test every surfactant and every salt of a monovalent cation, one of ordinary skill in the art would reasonably expect that other surfactants and other salts of a monovalent cation might be substituted.

Regarding statistical significance, the results shown in Table 1, item 10 on page 3 of the Majima Declaration are dramatic. There is hardly any fluorescence response at all for the 0.1M NaCl treatment while there is a sharp signal for both 0.5M NaCl and 2M NaCl. One of ordinary skill in the art would consider the results shown in the fluorescence trace of Table 1 to be significant.

M.P.E.P. 2144.05 also states that: "A *prima facie* case of obviousness may also be rebutted by showing that the art, in any material respect, teaches away from the claimed invention. *In re Geisler*, 116 F.3d 1465, 1471, 43 USPQ2d 1362, 1366 (Fed. Cir. 1997)...". Applicants have also provided evidence that the prior art taught avoidance of high salt for PCR work, so that one of ordinary skill in the art would not even consider the concentrations of salt used in the claimed method. Evidence for this position has been presented in previous responses and is supported by Chien (Journal of Bacteriology 127(3): 1550; submitted as attachment to response of 9/15/08 & 2/27/09).

Accordingly, Applicants have provided evidence both with a 132 Declaration to show criticality / unexpected results and with evidence teaching away from the claimed range. In addition, the claims are now amended to include the limitation that the samples are blood samples and that that the method steps are performed in the order as recited.

In view of Applicants' amendments and remarks, reconsideration and withdrawal of the above ground of rejection is respectfully requested.

No Disclaimers or Disavowals

Although the present communication may include alterations to the application or claims, or characterizations of claim scope or referenced art, Applicant is not conceding in this application that previously pending claims are not patentable over the cited references. Rather, any alterations or characterizations are being made to facilitate expeditious prosecution of this application. Applicant reserves the right to pursue at a later date any previously pending or other broader or narrower claims that capture any subject matter supported by the present disclosure, including subject matter found to be specifically disclaimed herein or by any prior prosecution. Accordingly, reviewers of this or any parent, child or related prosecution history shall not reasonably infer that Applicant has made any disclaimers or disavowals of any subject matter supported by the present application.

CONCLUSION

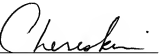
In view of Applicants' amendments to the claims and the foregoing Remarks, it is respectfully submitted that the present application is in condition for allowance. Should the Examiner have any remaining concerns which might prevent the prompt allowance of the application, the Examiner is respectfully invited to contact the undersigned at the telephone number appearing below.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: Dec. 28, 2009

By: 

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